AstraZeneca

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AstraZeneca welcome this opportunity to make known their views on Part 11 and the helpful guidance published in September last year. We have made vigorous efforts in the years since the original publication of Part 11 to bring our computer systems into line, not least because we believed that the majority of the rule was good common sense and value-adding both for patients and our business in terms of integrity and security. It was a 'wake-up call' both in terms of the restrictive demands it placed and the opportunities for efficiency in the 'e-world' that it provided.

Even so there have been challenges in meeting some of the technical demands and in justifying the application of the rule's logic to the total range of systems that seemed to be implicated. In this respect the 'Scope and Application' guidance was very welcome as an interim measure to alleviate these difficulties. There seemed to be a more logical focus offered and alternative options for resolution were made accessible. In particular we would like to give our support to the following 3 key areas.

1.ELIMINATE PRESCRIPTION

With a view to making full and good use of developing technology, we believe it is important that any revision of the rule which is forthcoming should not restrict choice, so the thrust of the new guidance to recommend gaining a better understanding of situations and functions through risk assessment, and then making decisions based on that together with a knowledge of the whole range of technology options, is to be applauded. We would be very much in favour of Part 11 enshrining the provisions of this latest guidance. In particular we believe that the Rule should not limit the way that objectives are achieved. In other words, it should define 'what' is required without defining 'how' with only a knowledge of 'today's solutions', and thus discouraging innovation. For example, the requirement for record conversion to preserve 'content and meaning' is, we feel, clear and adequate. Further development of this is likely to constrain options and is unnecessary. Similarly, § 11.10(d) calls for 'Limiting system access to authorized individuals', which is itself clear and unambiguous. A failure to achieve this is a non-compliance with the regulation and we would expect to investigate the situation as per § 211.100(b). To address this further in Part 11 seems an unnecessary complication. Again, to introduce concepts such as configuration management or document management in the context of § 11.10(k) restricts interpretation of 'appropriate controls', a phrase that combines usefully with the concept of risk-based logic.

2. NARROW SCOPE

The scope of Part 11 has been the subject of constant, energetic and heated discussion but now the emphasis of the interpretation onto records required under predicate rules or submitted to FDA has been very helpful in directing efforts into

areas of significant impact. Whilst responsible enterprises will make decisions as to what safeguards to apply based on their own assessment of absolute levels of impact, it would be generally helpful if the degree of explicitness of requirement within the predicate rules which is deemed to bring the record into scope could be further clarified. The much -quoted example of training records which are clearly necessary to demonstrate satisfactory compliance with § 211.25(a)&(b) but are not explicitly demanded is perhaps a case-in-point.
Similarly, another example is that 'written procedures' required by § 211.100(a) are treated by us as records, and therefore electronic records these days. Subpart J, though, does not include these in the description of 'Records and Reports' so are we perhaps mistaken and still making too broad an interpretation?

3. FULLY RISK-BASED
Closely related to the issue of narrowed scope, is the question of the application of a risk-based approach. The narrowed scope is itself, we believe, recognition that important areas defined by the predicate rules can be identified so that the requirements of the Rule can be applied only to these. Similarly the proper use of printed versions of those records negates the importance of the electronic version and allows conventional control methods. So, again, the guidance recognizes a valid and valuable principle.
Our proposal is that this principle can be applied to any real-life situation where neither judgement nor value is absolute. Any control should be applied commensurate to the risk it is designed to mitigate so that those raised in the 'request for comments' for example, operational system and device checks, could readily be included, although, even in the Rule as it is, the phrase 'as appropriate' already seems to allow this flexibility in §11.10(f) and (h)—but not in (g)! We understand the objective of keeping any aspect directly related to authority or authorization 'absolute', although there may even be circumstances that justify flexibility there? For Open systems it is arguable that §11.30 simply defines some of the 'how' for the particular case of systems where it is difficult, impracticable or impossible to control access adequately and so by applying risk-based logic to the situation this section becomes irrelevant. The objective "to ensure, as necessary under the circumstances, record authenticity, integrity, and confidentiality' is no different to that in §11.10.
Of course risk is a subjective concept and the guidance challenges us to make decisions based on "a justified and documented risk assessment, and a determination of the potential effect…"etc. Certainly any enterprise using the risk-based principle is going to have to clearly identify its process and parameters for judging risk as well as its methods for mitigating those risks, but please let us not have these prescribed, as methods and judgements change. The responsibility of the enterprise to justify the judgements to the Regulator is unavoidable and, whilst it can be scientifically based, it is important to recognize that there will still be a significant element of subjectivity.
"As appropriate" certainly has a very subjective feel to it whereas a mandated documented risk assessment sounds much more rigorous. However, we need to be careful that the effort does not outweigh the benefit and, worse, merely screen the

real dangers. We need to be sure it does not become mechanistic, driven by compliance demands, rather than the real benefits of focused effort.

In conclusion, it seems that the best test of compliance is not whether we can find a way to make the electronic system completely impenetrable to any challenge, but whether the net result of using the electronic system is at least as good as a paper equivalent. There may then be an expectation, driven at least for reasons of competitive advantage, that opportunities to build, through continuous improvement processes, will be taken. These will use developing, appropriately proven and value-adding technology, such as in document management and archiving for example, but there seems no purpose in regulating for what free-enterprise desires. Where paper records are generated by a computer system and suitably authenticated by human intervention there is every reason to accept these and not to try to apply further controls, as the test is met.

There are three main points that we believe to be key.

Firstly, that it is very important to meeting the objectives of this review--and indeed the original intent of the Rule—that it does not force a technique or technology to achieve a purpose which then limits our progress towards that objective. Let us remember that the aim is to ensure an adequate level of record and signature security, authenticity and integrity through innovation and the use of technological advances.

Secondly, that some further help on understanding the intent regarding how explicit the predicate rule requirements for record keeping have to be to be clear that they are in scope.

And finally, that the principle of risk management should be recognized throughout the Rule consistent with the concept that no judgement or control is absolute.

Thank you for this opportunity to contribute to the discussion on behalf of AstraZeneca.